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Placebos: Current Clinical Realities

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"In general, the placebo effect disappears when the patient knows he/she is receiving a placebo. This is in itself interesting, but since we believe in telling patients the truth, lying to patients in order to get the placebo effect presents an ethical conundrum."

"The use of placebos would be nullified if the patient knew. To use them when the patient does not know is unethical."

"As a physician trained in an environment which emphasized the importance of trust, and the validation of the individual's symptoms despite unexplainable physiology, I am opposed to the use of placebos even if research were to show benefit. The end does not justify the means."

INTRODUCTION

The power of the placebo effect was recognized in ancient times, as the following quotation from Socrates, according to Plato, illustrates: "[The cure for the headache] was a kind of leaf, which required to be accompanied by a charm, and if a person would repeat the charm at the same time that he used the cure, he would be made whole; but without the charm the leaf would be of no avail."¹

Placebos remain clinically relevant and philosophically interesting in the twenty-first century. While modern researchers often investigate placebos and the placebo effect within the context of experimental studies, there is little data on the current use of placebos in clinical practice. Our January 2008 study, "Academic Physicians Use Placebos in Clinical Practice and Believe in the Mind-Body Connection,"² is the first significant U.S. study on placebo use in clinical practice since 1979,³ other than a study of medicine interns from a single residency program published in 1999.⁴ Nearly half of the Chicago-based academic internists who responded to our survey reported using placebos in clinical practice, and nearly all believe in their therapeutic potential. Yet, the use of placebos outside of clinical trials is a source of ethical tension,⁵ as the three physician comments from our survey data (noted above the introduction) also illustrate.

In light of the ethical tension between harnessing the therapeutic power of the placebo and respecting patients' autonomy, and in the context of twenty-first century neuroscience hot in pursuit of the biological substrate of the mind-body connection,⁶ the publication of "Placebo Use in Clinical Practice: Report of the American Medical Association Council on Ethical and Judicial Affairs," in this issue of *JCE* is timely. It will,

no doubt, stimulate further discourse on the appropriate role of placebos in modern day medical practice. The AMA statement provides an initial set of guidelines regarding the ethical use of placebos and attempts to reconcile placebo use with modern principles of patient autonomy, informed consent, and non-deceptive therapeutic practices. As a fourth-year medical student and a family physician, neither an expert in medical ethics, we will comment on the AMA placebo statement primarily in the context of physicians' responses to our recent survey. The survey responses provide preliminary U.S. data about the current role of placebos in clinical practice.

EXAMINING THE AMA PLACEBO REPORT IN THE CONTEXT OF CURRENT PHYSICIANS' PRACTICES AND BELIEFS

We surveyed 466 academic internal medicine physicians in the Chicago area in the summer of 2006, and 50 percent responded.⁷ We asked physicians about their use of placebos and their knowledge, attitudes, and beliefs about the placebo effect. Physicians defined *placebo* in a variety of ways, but the most commonly agreed upon definition was *an intervention not considered to have a specific effect through a known physiologic mechanism*. Of the physicians we surveyed, 45 percent reported using placebos in clinical practice. Still, 12 percent said that placebo use should be categorically prohibited in clinical practice, while the rest supported the use of placebos in a variety of circumstances, including when research supports its efficacy (46 percent) and if the physician anticipates the placebo will benefit the patient (31 percent). About one in five respondents suggested placebo use was appropriate only after a patient was notified about "receiving a placebo." Of those who reported placebo use, when asked about their personal practice, 4 percent introduced the treatment using the word "placebo." Still, the majority offered information that may have accurately described the nature and purpose of the proposed treatment. For instance, 34 percent introduced the placebo as "a substance that may help you and will not hurt," and 9 percent as "medicine with no specific effect." Another 33 percent individualized their response to this question with statements such as, "This may help you but I am not sure how it works." At the time our data were collected, prior to the AMA report, psychiatrist Walter Brown proposed a way to introduce a placebo to patients that, he believed, avoided concerns about informed consent. Similar to most of our surveyed physicians, Brown's proposal, which he adapted from a previous study, does not explicitly contain the word *placebo*: "These pills do not contain any drug. We don't know exactly how they work; they may trigger or stimulate the body's own healing processes. . . ."⁸ According to our study results and Brown's recommendation, specific use of the word *placebo* is not a customary part of current clinical practice.

While our study offers new insight into physicians' behaviors and beliefs, our study is limited by its largely multiple-choice design, and further qualitative research is warranted to gain better insight into the nuances of individual physician's behaviors and attitudes. Still, many physician respondents offered comments that frequently referred to the tension between promoting the placebo effect and non-deceptive therapeutic practices. As a potential solution to what many physicians recognized as an "ethical conundrum," several physicians suggested that placebo use would be appropriate only if the patient agreed to the *possibility* of receiving a placebo. One physician commented, "As in a clinical trial, I would provide a placebo [in clinical practice] only if the patient knew that she/he may receive a placebo during the course of treatment, but may not know at what point during therapy. I think this would allow preservation of the placebo response." The AMA report offers a similar recommendation, stating that the patient must be informed and agree to receive a placebo for medical diagnosis or treatment, but the patient need not know the identity of the placebo at the actual time of use.

IS THE PLACEBO FOR THE PATIENT OR THE PHYSICIAN — OR BOTH?

The AMA report states that placebos "must not be given merely to mollify a difficult patient, because doing so serves the convenience of the physician more than it promotes the patient's welfare." In 1979, Goodwin, Goodwin, and Vogel found that 75 percent of the physicians surveyed had ordered a placebo for "a

'problem patient,' a patient that the nursing staff was complaining about."⁹ Although such use of placebos appears to be less common today, 15 percent of our physician respondents did report using placebos "after 'unjustified' demand for medication," and 6 percent had used a placebo "to get the patient to stop complaining." Rather than prescribing a placebo in these types of circumstances, the AMA encourages physicians to produce a "placebo-like effect through the skillful use of reassurance and encouragement." While reassurance and encouragement are indispensable physician practices and should be taught as a central part of medical schools' training courses on doctor-patient interaction, we believe there may be situations when a prescription for a placebo may *equally* serve the convenience of the physician and provide supplemental therapeutic benefit for the patient. This therapeutic value may be broadly conceived to apply to both disease-specific symptoms as well as personality-dependent emotional states that contribute to a patient's overall health, and may also influence disease-specific health outcomes.

THE USE OF "IMPURE" PLACEBOS

Although the AMA report acknowledges the potential use of pharmacologically active medications as placebos, it does not discuss the ethical implications of this practice. According to the AMA report, a placebo may be defined as a substance that has "no known specific pharmacological activity against the condition being treated." The use of a pharmacologically active medication for non-indicated conditions raises important ethical questions. For the purposes of our discussion, we will refer to pharmacologically active placebos as "impure placebos," a term used by professor of law Adam Kolber, who, in contrast, called a biologically inert substance a "pure placebo." Kolber writes, "Impure placebos can be difficult to detect because the prescribed medication has a pharmacological effect on some illnesses, and doctors may be able to provide plausible-sounding medical rationales for prescribing impure placebos."¹⁰

Our study found that physicians rarely prescribed "pure placebos." Rather, nearly all of the physicians who said they had prescribed a placebo prescribed "impure placebos." Of the 48 percent of physicians who reported giving at least one type of treatment in a situation when there was no evidence of clinical efficacy. Among the treatments given, 33 percent reported giving antibiotics for viral or other nonbacterial diagnoses, others gave vitamins (20 percent), ibuprofen (12 percent), sub-therapeutic doses of medication (7 percent), and herbal supplements (5 percent). Only a small minority of physicians reported giving what may be considered "pure placebos," such as prepared placebo tablets (2 percent), saline infusions (3 percent), and sugar or artificial sweetener pills (1 percent). These results suggest that the placebos used by physicians in clinical practice are rarely biologically inert substances, or "dummy" pills, which is how they are typically characterized in research trials and in popular culture. Unfortunately, "impure placebos" may have known potential negative side-effects and, in the case of antibiotics, their overuse promotes drug-resistant infections. We believe further dialogue regarding the appropriate use of "impure placebos" in clinical practice is needed.

PLACEBOS AS SYMBOLS OF HEALING

A placebo serves as a symbol of healing that triggers positive therapeutic expectations in a patient. We suggest that the definition of placebos include but not be limited to a "substance," as defined by the AMA report. We suggest the definition of placebos also include interventions or factors that have no known specific clinical efficacy against the condition being treated. Physicians' practices such as wearing a white coat, or the physical examination of the patient (independent of diagnostic purposes) may serve as placebo treatments for patients. As one physician in our study commented, "I have always wondered if the office physical exam is as much a sophisticated grooming ritual to relieve stress rather than obtain diagnostic information. In the outpatient setting it is typically normal but both physician and patient are fairly attached to its performance."

In another example of the symbolic value of a placebo, physician David Watts, a gastroenterologist, poet, and writer, spoke of his experience *prescribing* medication to patients that he also suggested they may not need to take. "There's something about sitting down at the desk and writing it [the medication] out

longhand, tearing the prescription from its pad and handing it to him [the patient], taking it down to the pharmacist who brings forth this amber bottle with a childproof cap and 25 small white excretions of something wonderful. Something about all of that that is just the right amount."¹¹ This expanded definition of a placebo captures the broader symbolic aspects of patient care that may trigger the placebo effect.

CONCLUSION

As a matter of scientific inquiry, the power of the placebo effect will continue to be researched as an isolated variable, both in formal research studies and during *N-of-1* clinical trials (trials in which a medication is tested in only one individual). Ultimately, in clinical practice, the separation of placebos and the placebo effect from other forms of therapy is somewhat artificial. In the context of everyday medicine, we believe the symbolic value of placebos and the power of the placebo effect are best served not as isolated therapeutic tools, but rather as integrated aspects of humanistic and holistic patient care. In the year 2008, amidst great technological advances of modern medicine, the purpose of the ancient charm used by Socrates still resonates. "For the charm will do more, Charmides, than only cure the headache. I dare say that you have heard eminent physicians say to a patient who comes to them with bad eyes, that they cannot cure his eyes by themselves, but that if his eyes are to be cured, his head must be treated; and then again they say that to think of curing the head alone, and not the rest of the body also, is the height of folly. And arguing in this way they apply their methods to the whole body, and try to treat and heal the whole and the part together."¹²

POSSIBLE ADDENDA TO THE AMA RECOMMENDATIONS ON PLACEBO

We offer the following as possible additions to the AMA report.

1. Placebos, when used, should be a supplement and not a substitute for a clinically indicated treatment.
2. Placebos may be useful when there is no other effective treatment available for a patient.
3. "Pure" placebos are generally safer than "impure" placebos.
4. Only safe impure placebos should be used (for example, certain vitamins).

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NOTES

The quotations at the beginning of this article are anonymous physicians' quotes from the authors' 2006 survey data.

1. Plato, "Charmides, or Temperance," trans. B. Jowett, *Internet Classics Archive*, <http://classics.mit.edu/Plato/charmides.html>.

2. R. Sherman and J. Hickner, "Academic physicians use placebos in clinical practice and believe in the mind-body connection," *Journal of General Internal Medicine* 23 (2008): 7-10.

3. J.S. Goodwin, J.M. Goodwin, and A.V. Vogel, "Knowledge and use of placebos by house officers and nurses," *Annals of Internal Medicine* 91, no. 1 (1979): 106-10.

4. J.T. Berger, "Placebo medication use in patient care: A survey of medical interns," *Western Journal of Medicine* 170, no. 2 (1999): 93-6.

5. S. Bok, "Ethical issues in use of placebo in medical practice and clinical trials," in *The science of the placebo: toward an interdisciplinary research agenda*, ed. H.A. Guess et al. (London: BMJ Books, 2002), 53-74.

6. F. Benedetti et al., "Neurobiological Mechanisms of the Placebo Effect," *Journal of Neuroscience* 25, no. 45 (2005): 10390-402.

7. See note 2 above.

8. W. Brown, "Placebo as a treatment for depression," *Neuropsychopharmacology* 10, no. 4 (1994): 265-9; L.C. Park and L. Covi, "Non-blind placebo trial: an exploration of neurotic patients' responses to placebo when its inert content is disclosed," *Archives of General Psychiatry* 12 (1965): 36-45.

9. Goodwin, Goodwin, and Vogel, see note 3 above.

10. A.J. Kolber, "A Limited Defense of Clinical Placebo Deception," *Yale Law and Policy Review* 26 (2007).

11. D. Watts, "Commentary: Placebo Effect," *Your Health*, NPR, 6 August 2003.

12. See note 1 above.